SEQUENCE LISTING

<110>   Pecker, Iris
        Vlodavsky , Israel
        Feinstein, Elena

<120>   POLYNUCLEOTIDE ENCODING A POLYPEPTIDE HAVING HEPARANASE ACTIVITY AND EXPRESSION
OF SAME IN GENETICALLY MODIFIED CELLS

<130>   01/22603

<150>   US 08/922,170
<151>   1997-09-02

<150>   US 09/109,386
<151>   1998-07-10

<150>   PCT/US98/17954
<151>   1998-08-31

<160>   47

<170>   PatentIn version 3.1

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acctggactt cttcacccag gagccgctgc acctggtgag cccctcgttc ctgtccgtca   240

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ctcaagtcaa ccaggatatt tgcaaatatg gatccatccc tcctgatgtg gaggagaagt   480

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            20                  25                  30


Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro
            35                  40                  45


Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
        50                  55                  60


Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
65                  70                  75                  80


Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
                85                  90                  95


Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe
                100                 105                 110
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Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys Lys
115   120   125

Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu Trp
130   135   140

Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys Phe
145   150   155   160

Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe
                165   170   175

Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu
            180   185   190

Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
        195   200   205

Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn
    210   215   220

Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser
225   230   235   240

Gln Leu Gly Glu Asp Tyr Ile Gln Leu His Lys Leu Leu Arg Lys Ser
            245   250   255

Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg
            260   265   270

Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu
        275   280   285

Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr
    290   295   300

Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile
305   310   315   320

Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly
            325   330   335

Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala
            340   345   350

Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys
        355   360   365

Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val
    370   375   380

Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro
385   390   395   400

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Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr
            405             410             415

Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg
            420             425             430

Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly
        435             440             445

Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu
    450             455             460

Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu
465             470             475             480

Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn
            485             490             495

Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met
        500             505             510

Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser
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Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile
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   Met Leu Leu Arg Ser Lys Pro Ala Leu Pro Pro Pro Leu Met Leu
   1               5                   10                  15

ctg ctc ctg ggg ccg ctg ggt ccc ctc tcc cct ggc gcc ctg ccc cga    155
Leu Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg
                20              25                  30

cct gcg caa gca cag gac gtc gtg gac ctg gac ttc ttc acc cag gag    203
Pro Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu
            35              40                  45

ccg ctg cac ctg gtg agc ccc tcg ttc ctg tcc gtc acc att gac gcc    251
Pro Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala
        50              55                  60

aac ctg gcc acg gac ccg cgg ttc ctc atc ctc ctg ggt tct cca aag    299
Asn Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys
        65              70              75

ctt cgt acc ttg gcc aga ggc ttg tct cct gcg tac ctg agg ttt ggt    347
Leu Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly
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	80				85					90					95			

ggc acc aag aca gac ttc cta att ttc gat ccc aag aag gaa tca acc   395
Gly Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr
            100   105   110

ttt gaa gag aga agt tac tgg caa tct caa gtc aac cag gat att tgc   443
Phe Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys
               115   120   125

aaa tat gga tcc atc cct cct gat gtg gag gag aag tta cgg ttg gaa   491
Lys Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu
          130   135   140

tgg ccc tac cag gag caa ttg cta ctc cga gaa cac tac cag aaa aag   539
Trp Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys
       145   150   155

ttc aag aac agc acc tac tca aga agc tct gta gat gtg cta tac act   587
Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr
160   165   170   175

ttt gca aac tgc tca gga ctg gac ttg atc ttt ggc cta aat gcg tta   635
Phe Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu
             180   185   190

tta aga aca gca gat ttg cag tgg aac agt tct aat gct cag ttg ctc   683
Leu Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu
             195   200   205

ctg gac tac tgc tct tcc aag ggg tat aac att tct tgg gaa cta ggc   731
Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly
          210   215   220

aat gaa cct aac agt ttc ctt aag aag gct gat att ttc atc aat ggg   779
Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly
        225   230   235

tcg cag tta gga gaa gat tat att caa ttg cat aaa ctt cta aga aag   827
Ser Gln Leu Gly Glu Asp Tyr Ile Gln Leu His Lys Leu Leu Arg Lys
240   245   250   255

tcc acc ttc aaa aat gca aaa ctc tat ggt cct gat gtt ggt cag cct   875
Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro
             260   265   270

cga aga aag acg gct aag atg ctg aag agc ttc ctg aag gct ggt gga   923
Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly
         275   280   285

gaa gtg att gat tca gtt aca tgg cat cac tac tat ttg aat gga cgg   971
Glu Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg
        290   295   300

act gct acc agg gaa gat ttt cta aac cct gat gta ttg gac att ttt   1019
Thr Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe
       305   310   315

att tca tct gtg caa aaa gtt ttc cag gtg gtt gag agc acc agg cct   1067
Ile Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro
320   325   330   335

ggc aag aag gtc tgg tta gga gaa aca agc tct gca tat gga ggc gga   1115
Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly
             340   345   350

gcg ccc ttg cta tcc gac acc ttt gca gct ggc ttt atg tgg ctg gat   1163
Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp
             355   360   365

aaa ttg ggc ctg tca gcc cga atg gga ata gaa gtg gtg atg agg caa   1211
Lys Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln
       370   375   380

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Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp
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cct tta cct gat tat tgg cta tct ctt ctg ttc aag aaa ttg gtg ggc      1307
Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly
400             405             410             415

acc aag gtg tta atg gca agc gtg caa ggt tca aag aga agg aag ctt      1355
Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu
            420             425             430

cga gta tac ctt cat tgc aca aac act gac aat cca agg tat aaa gaa      1403
Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu
            435             440             445

gga gat tta act ctg tat gcc ata aac ctc cat aac gtc acc aag tac      1451
Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr
            450             455             460

ttg cgg tta ccc tat cct ttt tct aac aag caa gtg gat aaa tac ctt      1499
Leu Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu
    465             470             475

cta aga cct ttg gga cct cat gga tta ctt tcc aaa tct gtc caa ctc      1547
Leu Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu
480             485             490             495

aat ggt cta act cta aag atg gtg gat gat caa acc ttg cca cct tta      1595
Asn Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu
            500             505             510

atg gaa aaa cct ctc cgg cca gga agt tca ctg ggc ttg cca gct ttc      1643
Met Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe
            515             520             525

tca tat agt ttt ttt gtg ata aga aat gcc aaa gtt gct gct tgc atc      1691
Ser Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile
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tgggcataga agtcgtgatg aggcaggtgt tcttcggagc aggcaactac cacttagtgg     180

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gaaatgccaa aatcgctgct tgtatatgaa aataaaaggc atacggtacc cctgagacaa     660

aagccgaggg gggtgttatt cataaaacaa aaccctagtt taggaggcca cctccttgcc     720
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gagttccaga gcttcgggag ggtgggtac acttcagtat tacattcagt gtggtgttct   780

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aggcgtaacg gggcggagga aaggagaaaa gggcgctggg gctcggcggg aggaagtgct   180

agagctctcg actctccgct gcgcggcagc tggcggggggg agcagccagg tgagcccaag   240

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agcttcctga aggctggtgg agaagtgatt gattcagtta catggcatca ctactatttg   1140

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        35   40   45

Lys Met Leu Leu Arg Ser Lys Pro Ala Leu Pro Pro Pro Leu Met Leu
    50   55   60

Leu Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg
65   70   75   80

Pro Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu
                85   90   95

Pro Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala
            100   105   110

Asn Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys
            115   120   125

Leu Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly
        130   135   140

Gly Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr
145   150   155   160

Phe Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys
                165   170   175

Lys Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu
            180   185   190

Trp Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys
        195   200   205

Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr
    210   215   220

Phe Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu
225   230   235   240

Leu Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu

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                290                295                300

        Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro
        305                310                315                320

        Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly
                    325                330                335

        Glu Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg
                    340                345                350

        Thr Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe
                    355                360                365

        Ile Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro
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        385                390                395                400

        Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp
                    405                410                415

        Lys Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln
                    420                425                430

        Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp
                    435                440                445
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        Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly
                450                455                460

        Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu
        465                470                475                480

        Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu
                    485                490                495

        Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr
                    500                505                510

        Leu Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu
                515                520                525

        Leu Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu
        530                535                540
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Asn Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu
545             550             555             560


Met Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe
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Ser Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile
            580             585             590
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<210> 15
<211> 1899
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<213> Homo sapiens

<220>
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<222> (94)..(1869)
<223>

<400> 15

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cagtgggagg gatgcagaag aggagtggga ggg atg gag ggc gca gtg gga ggg     114
                                     Met Glu Gly Ala Val Gly Gly
                                     1               5

gtg agg agg cgt aac ggg gcg gag gaa agg aga aaa ggg cgc tgg ggc     162
Val Arg Arg Arg Asn Gly Ala Glu Glu Arg Arg Lys Gly Arg Trp Gly
        10              15              20

tcg gcg gga gga agt gct aga gct ctc gac tct ccg ctg cgc ggc agc     210
Ser Ala Gly Gly Ser Ala Arg Ala Leu Asp Ser Pro Leu Arg Gly Ser
    25              30              35

tgg cgg ggg gag cag cca ggt gag ccc aag atg ctg ctg cgc tcg aag     258
Trp Arg Gly Glu Gln Pro Gly Glu Pro Lys Met Leu Leu Arg Ser Lys
40              45              50              55

cct gcg ctg ccg ccg ccg ctg atg ctg ctg ctc ctg ggg ccg ctg ggt     306
Pro Ala Leu Pro Pro Pro Leu Met Leu Leu Leu Leu Gly Pro Leu Gly
                60              65              70

ccc ctc tcc cct ggc gcc ctg ccc cga cct gcg caa gca cag gac gtc     354
Pro Leu Ser Pro Gly Ala Leu Pro Arg Pro Ala Gln Ala Gln Asp Val
            75              80              85

gtg gac ctg gac ttc ttc acc cag gag ccg ctg cac ctg gtg agc ccc     402
Val Asp Leu Asp Phe Phe Thr Gln Glu Pro Leu His Leu Val Ser Pro
            90              95              100

tcg ttc ctg tcc gtc acc att gac gcc aac ctg gcc acg gac ccg cgg     450
Ser Phe Leu Ser Val Thr Ile Asp Ala Asn Leu Ala Thr Asp Pro Arg
    105             110             115

ttc ctc atc ctc ctg ggt tct cca aag ctt cgt acc ttg gcc aga ggc     498
Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu Arg Thr Leu Ala Arg Gly
120             125             130             135

ttg tct cct gcg tac ctg agg ttt ggt ggc acc aag aca gac ttc cta     546
Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu
                140             145             150

att ttc gat ccc aag aag gaa tca acc ttt gaa gag aga agt tac tgg     594
Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe Glu Glu Arg Ser Tyr Trp
                155             160             165

caa tct caa gtc aac cag gat att tgc aaa tat gga tcc atc cct cct     642
Gln Ser Gln Val Asn Gln Asp Ile Cys Lys Tyr Gly Ser Ile Pro Pro
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                170                 175                 180

gat gtg gag gag aag tta cgg ttg gaa tgg ccc tac cag gag caa ttg     690
Asp Val Glu Glu Lys Leu Arg Leu Glu Trp Pro Tyr Gln Glu Gln Leu
    185                 190                 195

cta ctc cga gaa cac tac cag aaa aag ttc aag aac agc acc tac tca     738
Leu Leu Arg Glu His Tyr Gln Lys Lys Phe Lys Asn Ser Thr Tyr Ser
200                 205                 210                 215

aga agc tct gta gat gtg cta tac act ttt gca aac tgc tca gga ctg     786
Arg Ser Ser Val Asp Val Leu Tyr Thr Phe Ala Asn Cys Ser Gly Leu
                220                 225                 230

gac ttg atc ttt ggc cta aat gcg tta tta aga aca gca gat ttg cag     834
Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Ala Asp Leu Gln
                235                 240                 245

tgg aac agt tct aat gct cag ttg ctc ctg gac tac tgc tct tcc aag     882
Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys
                250                 255                 260

ggg tat aac att tct tgg gaa cta ggc aat gaa cct aac agt ttc ctt     930
Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Leu
    265                 270                 275

aag aag gct gat att ttc atc aat ggg tcg cag tta gga gaa gat tat     978
Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser Gln Leu Gly Glu Asp Tyr
280                 285                 290                 295

att caa ttg cat aaa ctt cta aga aag tcc acc ttc aaa aat gca aaa    1026
Ile Gln Leu His Lys Leu Leu Arg Lys Ser Thr Phe Lys Asn Ala Lys
                300                 305                 310

ctc tat ggt cct gat gtt ggt cag cct cga aga aag acg gct aag atg    1074
Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg Arg Lys Thr Ala Lys Met
                315                 320                 325

ctg aag agc ttc ctg aag gct ggt gga gaa gtg att gat tca gtt aca    1122
Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Val Thr
                330                 335                 340

tgg cat cac tac tat ttg aat gga cgg act gct acc agg gaa gat ttt    1170
Trp His His Tyr Tyr Leu Asn Gly Arg Thr Ala Thr Arg Glu Asp Phe
    345                 350                 355

cta aac cct gat gta ttg gac att ttt att tca tct gtg caa aaa gtt    1218
Leu Asn Pro Asp Val Leu Asp Ile Phe Ile Ser Ser Val Gln Lys Val
360                 365                 370                 375

ttc cag gtg gtt gag agc acc agg cct ggc aag aag gtc tgg tta gga    1266
Phe Gln Val Val Glu Ser Thr Arg Pro Gly Lys Lys Val Trp Leu Gly
                380                 385                 390

gaa aca agc tct gca tat gga ggc gga gcg ccc ttg cta tcc gac acc    1314
Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asp Thr
                395                 400                 405

ttt gca gct ggc ttt atg tgg ctg gat aaa ttg ggc ctg tca gcc cga    1362
Phe Ala Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Arg
                410                 415                 420

atg gga ata gaa gtg gtg atg agg caa gta ttc ttt gga gca gga aac    1410
Met Gly Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn
    425                 430                 435

tac cat tta gtg gat gaa aac ttc gat cct tta cct gat tat tgg cta    1458
Tyr His Leu Val Asp Glu Asn Phe Asp Pro Leu Pro Asp Tyr Trp Leu
440                 445                 450                 455

tct ctt ctg ttc aag aaa ttg gtg ggc acc aag gtg tta atg gca agc    1506
Ser Leu Leu Phe Lys Lys Leu Val Gly Thr Lys Val Leu Met Ala Ser
                460                 465                 470
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gtg caa ggt tca aag aga agg aag ctt cga gta tac ctt cat tgc aca    1554
Val Gln Gly Ser Lys Arg Arg Lys Leu Arg Val Tyr Leu His Cys Thr
            475                 480                 485

aac act gac aat cca agg tat aaa gaa gga gat tta act ctg tat gcc    1602
Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly Asp Leu Thr Leu Tyr Ala
            490                 495                 500

ata aac ctc cat aac gtc acc aag tac ttg cgg tta ccc tat cct ttt    1650
Ile Asn Leu His Asn Val Thr Lys Tyr Leu Arg Leu Pro Tyr Pro Phe
        505                 510                 515

tct aac aag caa gtg gat aaa tac ctt cta aga cct ttg gga cct cat    1698
Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu Arg Pro Leu Gly Pro His
520                 525                 530                 535

gga tta ctt tcc aaa tct gtc caa ctc aat ggt cta act cta aag atg    1746
Gly Leu Leu Ser Lys Ser Val Gln Leu Asn Gly Leu Thr Leu Lys Met
                540                 545                 550

gtg gat gat caa acc ttg cca cct tta atg gaa aaa cct ctc cgg cca    1794
Val Asp Asp Gln Thr Leu Pro Pro Leu Met Glu Lys Pro Leu Arg Pro
                555                 560                 565

gga agt tca ctg ggc ttg cca gct ttc tca tat agt ttt ttt gtg ata    1842
Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser Tyr Ser Phe Phe Val Ile
            570                 575                 580

aga aat gcc aaa gtt gct gct tgc atc tgaaaataaa atatactagt          1889
Arg Asn Ala Lys Val Ala Ala Cys Ile
        585                 590

cctgacactg                                                         1899
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<213>  Homo sapiens

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tttttttcagg caaaagtaaa atacctgaga aactgcctgg ccagaggaca atcagatttt   180

ggctggctca agtgacaagc aagtgtttat aagctagatg ggagaggaag ggatgaatac   240

tccattggag gctttactcg agggtcagag ggatacccgg cgccatcaga atgggatctg   300

ggagtcggaa acgctgggtt cccacgagag cgcgcagaac acgtgcgtca ggaagcctgg   360

tccgggatgc ccagcgctgc tccccgggcg ctcctccccg ggcgctcctc cccaggcctc   420

ccgggcgctt ggatcccggc catctccgca cccttcaagt gggtgtgggt gatttcgtaa   480

gtgaacgtga ccgccaccgg ggggaaagcg agcaaggaag taggagagag ccgggcaggc   540

ggggcggggt tggattggga gcagtgggag ggatgcagaa gaggagtggg aggg          594
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<213>  Artificial sequence

<220>
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<211>  21
<212>  DNA
<213>  Artificial sequence

<220>
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<211>  22
<212>  DNA
<213>  Artificial sequence

<220>
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<400>  19                                                          22
gtaatacgac tcactatagg gc
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<220>
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<400>  20                                                          19
actatagggc acgcgtggt
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agctctgtag atgtgctata cac
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gagcagccag gtgagcccaa gat


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ttcgatccca agaaggaatc aac


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gcatcttagc cgtctttctt cg


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gtagtgatgc catgtaactg aatc
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<220>
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<210>  32
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<220>
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<400>  32
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<220>
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<400>  33
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<210>  34
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<220>
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<400>  34
gccagctgca aaggtgttgg ac                                           22


<210>  35
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<212>  DNA
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<220>
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<400>  35
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<210>  36
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<220>
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<400>    36
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<210>    37
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<400>    37
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<210>    38
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<400>    38
gtaatacgac tcactatagg gc                                    22


<210>    39
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<212>    DNA
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<400>    39
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<210>    40
<211>    27
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<400>    40
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<210>    41
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<400>    41
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<210>    42
<211>    44848
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<212> DNA
<213> Homo sapiens

<400> 42

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ttgaactctt gggctctagt gatccacccg ccttggcctc ccaaagtgct gggattacag       180

gtgtgagcca tcacacccgg ccccccgttt ccatattagt aactcacatg tagaccacaa       240

ggatgcacta tttagaaaac ttgcaatggt ccacttttca aatcacccaa acatgttaaa       300

gaaattggta tgactgggca tggcacagtg gctcatgcct gcaatcctag cattttgtga       360

ggctgagacg ggcagatcac gaggtcagga gattgagacc atcctgacag acatggtgaa       420

atcccatctc tactaaaaat acaaaacaat tagccggggg tgatggcagg cccctgtagt       480

cccagctact cgggaggctg aggcaggaga atggcgtgaa tccaggaggc agagcttgca       540

gtgagccgag atggtgccac tgcactccag cctgggcgac agagcgagac tccgtctcaa       600

aaaaaaaaaa aaagaaagaa attggtatga ctgttgactc acaacaggag tcaggggcat       660

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gcgtgagtcc ctcgttcctg tccatcacca tcgacgccag cctggccacc gacccgcgct    780
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tcctcacctt cctgggctct ccaaggctcc gtgctctggc tagaggctta tctcctgcat    840

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cttccgaaga aagaagttac tggaaatctc aagtcaacca tgatatttgc aggtctgagc    960

cggtctctgc tgcggtgttg aggaaactcc aggtggaatg gcccttccag gagctgttgc   1020

tgctccgaga gcagtaccaa aaggagttca agaacagcac ctactcaaga agctcagtgg   1080

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tactacgaac cccagactta cggtggaaca gctccaacgc ccagcttctc cttgactact   1200

gctcttccaa gggttataac atctcctggg aactgggcaa tgagcccaac agtttctgga   1260

agaaagctca cattctcatc gatgggttgc agttaggaga agactttgtg gagttgcata   1320

aacttctaca aaggtcagct ttccaaaatg caaaactcta tggtcctgac atcggtcagc   1380

ctcgagggaa gacagttaaa ctgctgagga gtttcctgaa ggctggcgga gaagtgatcg   1440

actctcttac atggcatcac tattacttga atggacgcat cgctaccaaa gaagattttc   1500

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gtgcaccctt gctgtccaac acctttgcag ctggctttat gtggctggat aaattgggcc   1680

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cccctgagac aaaagccgag gggggtgtta ttcataaaac aaaaccctag tttaggaggc   2280

cacctccttg ccgagttcca gagcttcggg agggtggggt acacttcagt attacattca   2340

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                20                  25                  30


Leu Glu Phe Tyr Thr Lys Arg Pro Leu Arg Ser Val Ser Pro Ser Phe
            35                  40                  45
```

Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu
    50   55   60

Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser
65   70   75   80

Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe
            85   90   95

Asp Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser
            100   105   110

Gln Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val
        115   120   125

Leu Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu
    130   135   140

Arg Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser
145   150   155   160

Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu
            165   170   175

Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn
            180   185   190

Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr
        195   200   205

Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys Lys
    210   215   220

Ala His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu
225   230   235   240

Leu His Lys Leu Leu Gln Arg Ser Ala Phe Gln Asn Ala Lys Leu Tyr
            245   250   255

Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu Arg
            260   265   270

Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp His
            275   280   285

His Tyr Tyr Leu Asn Gly Arg Ile Ala Thr Lys Glu Asp Phe Leu Ser
    290   295   300

Ser Asp Ala Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu Lys
305   310   315   320

Val Thr Lys Glu Ile Thr Pro Gly Lys Lys Val Trp Leu Gly Glu Thr
            325   330   335

```
Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe Ala
        340             345             350

Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Met Gly
        355             360             365

Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His
    370             375             380

Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu
385             390             395             400

Leu Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys
            405             410             415

Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val
            420             425             430

Tyr His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn
        435             440             445

Leu His Asn Val Thr Lys His Leu Lys Val Pro Pro Pro Leu Phe Arg
    450             455             460

Lys Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu
465             470             475             480

Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp
            485             490             495

Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly Ser
        500             505             510

Ala Leu Ser Leu Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg Asn
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Ala Lys Ile Ala Ala Cys Ile
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ttaaggcaga agggagtcgg ggtagggtct ggctgaaccc tcaaccgggg cttttaactc    180

agggtctagt cctggcgcca aatggatggg acctagaaaa ggtgacagag tgcgcaggac    240

accaggaagc tggtcccacc cctgcgcggc tcccgggcgc tccctcccca ggcctccgag    300
```

```
gatcttggat tctggccacc tccgcaccct ttggatgggt gtggatgatt tcaaaagtgg    360

acgtgaccgc ggcggagggg aaagccagca cggaaatgaa agagagcgag gaggggaggg    420

cggggagggg agggcgctag ggagggactc ccgggagggg tgggagggat ggagcgctgt    480

gggagggtac tgagtcctgg cgccagaggc gaagcaggac cggttgcagg gggcttgagc    540

cagcgcgccg gctgccccag ctctcccggc agcgggcggt ccagccaggt ggg atg       596
                                                             Met
                                                             1
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```
ctg agg ctg ctg ctg ctg tgg ctc tgg ggg ccg ctc ggt gcc ctg gcc    644
Leu Arg Leu Leu Leu Leu Trp Leu Trp Gly Pro Leu Gly Ala Leu Ala
        5                   10                  15
```

```
cag ggc gcc ccc gcg ggg acc gcg ccg acc gac gac gtg gta gac ttg    692
Gln Gly Ala Pro Ala Gly Thr Ala Pro Thr Asp Asp Val Val Asp Leu
        20                  25                  30
```

```
gag ttt tac acc aag cgg ccg ctc cga agc gtg agt ccc tcg ttc ctg    740
Glu Phe Tyr Thr Lys Arg Pro Leu Arg Ser Val Ser Pro Ser Phe Leu
    35                  40                  45
```

```
tcc atc acc atc gac gcc agc ctg gcc acc gac ccg cgc ttc ctc acc    788
Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu Thr
50                  55                  60                  65
```

```
ttc ctg ggc tct cca agg ctc cgt gct ctg gct aga ggc tta tct cct    836
Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser Pro
                70                  75                  80
```

```
gca tac ttg aga ttt ggc ggc aca aag act gac ttc ctt att ttt gat    884
Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe Asp
                85                  90                  95
```

```
ccg gac aag gaa ccg act tcc gaa gaa aga agt tac tgg aaa tct caa    932
Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser Gln
            100                 105                 110
```

```
gtc aac cat gat att tgc agg tct gag ccg gtc tct gct gcg gtg ttg    980
Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val Leu
        115                 120                 125
```

```
agg aaa ctc cag gtg gaa tgg ccc ttc cag gag ctg ttg ctg ctc cga   1028
Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu Arg
130                 135                 140                 145
```

```
gag cag tac caa aag gag ttc aag aac agc acc tac tca aga agc tca   1076
Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser
                150                 155                 160
```

```
gtg gac atg ctc tac agt ttt gcc aag tgc tcg ggg tta gac ctg atc   1124
Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu Ile
                165                 170                 175
```

```
ttt ggt cta aat gcg tta cta cga acc cca gac tta cgg tgg aac agc   1172
Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn Ser
                180                 185                 190
```

```
tcc aac gcc cag ctt ctc ctt gac tac tgc tct tcc aag ggt tat aac   1220
Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn
        195                 200                 205
```

```
atc tcc tgg gaa ctg ggc aat gag ccc aac agt ttc tgg aag aaa gct   1268
Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys Lys Ala
210                 215                 220                 225
```

```
cac att ctc atc gat ggg ttg cag tta gga gaa gac ttt gtg gag ttg   1316
His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu Leu
                230                 235                 240
```

```
cat aaa ctt cta caa agg tca gct ttc caa aat gca aaa ctc tat ggt      1364
His Lys Leu Leu Gln Arg Ser Ala Phe Gln Asn Ala Lys Leu Tyr Gly
            245                 250                 255

cct gac atc ggt cag cct cga ggg aag aca gtt aaa ctg ctg agg agt      1412
Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu Arg Ser
            260                 265                 270

ttc ctg aag gct ggc gga gaa gtg atc gac tct ctt aca tgg cat cac      1460
Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp His His
            275                 280                 285

tat tac ttg aat gga cgc atc gct acc aaa gaa gat ttt ctg agc tct      1508
Tyr Tyr Leu Asn Gly Arg Ile Ala Thr Lys Glu Asp Phe Leu Ser Ser
290                 295                 300                 305

gat gcg ctg gac act ttt att ctc tct gtg caa aaa att ctg aag gtc      1556
Asp Ala Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu Lys Val
            310                 315                 320

act aaa gag atc aca cct ggc aag aag gtc tgg ttg gga gag acg agc      1604
Thr Lys Glu Ile Thr Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser
            325                 330                 335

tca gct tac ggt ggc ggt gca ccc ttg ctg tcc aac acc ttt gca gct      1652
Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe Ala Ala
            340                 345                 350

ggc ttt atg tgg ctg gat aaa ttg ggc ctg tca gcc cag atg ggc ata      1700
Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Met Gly Ile
            355                 360                 365

gaa gtc gtg atg agg cag gtg ttc ttc gga gca ggc aac tac cac tta      1748
Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His Leu
370                 375                 380                 385

gtg gat gaa aac ttt gag cct tta cct gat tac tgg ctc tct ctt ctg      1796
Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu
            390                 395                 400

ttc aag aaa ctg gta ggt ccc agg gtg tta ctg tca aga gtg aaa ggc      1844
Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys Gly
            405                 410                 415

cca gac agg agc aaa ctc cga gtg tat ctc cac tgc act aac gtc tat      1892
Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val Tyr
            420                 425                 430

cac cca cga tat cag gaa gga gat cta act ctg tat gtc ctg aac ctc      1940
His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn Leu
            435                 440                 445

cat aat gtc acc aag cac ttg aag gta ccg cct ccg ttg ttc agg aaa      1988
His Asn Val Thr Lys His Leu Lys Val Pro Pro Pro Leu Phe Arg Lys
450                 455                 460                 465

cca gtg gat acg tac ctt ctg aag cct tcg ggg ccg gat gga tta ctt      2036
Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu Leu
            470                 475                 480

tcc aaa tct gtc caa ctg aac ggt caa att ctg aag atg gtg gat gag      2084
Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp Glu
            485                 490                 495

cag acc ctg cca gct ttg aca gaa aaa cct ctc ccc gca gga agt gca      2132
Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly Ser Ala
            500                 505                 510

cta agc ctg cct gcc ttt tcc tat ggt ttt ttt gtc ata aga aat gcc      2180
Leu Ser Leu Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg Asn Ala
            515                 520                 525

aaa atc gct gct tgt ata tgaaaataaa aggcatacgg tacccctgag             2228
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Lys Ile Ala Ala Cys Ile
530                 535
```

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acaaaagccg aggggggtgt tattcataaa acaaaaccct agtttaggag gccacctcct    2288

tgccgagttc cagagcttcg ggagggtggg gtacacttca gtattacatt cagtgtggtg    2348

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cggttcctca ccttcctgag ctctccacgg cttcgagccc tgtctagagg cttatctcct     240

gcgtacttga gatttggcgg caccaagact gacttcctta tttttgatcc caacaacgaa     300

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cattaactgt caccacctgc agtggtctac ttagagaaca ccgcactgga tgttaacact     180

gaagcgcgtg ccccgccctc ccgaggctct ggatccagcg ttgaagcttg ccccgccctc     240

ccgaggctct ggatccagca ctggagcatg ccccgccctc ccgaggctct ggagcttgct     300

aaggagtccg ctccctaccg ctggggtttt gctttattct tatgaatgac acccctgacc     360

gctttcgtct caggggtact gtaatgcctt ttattttcat atacaagctg cgattttggc     420

atttcttatg acaaaaaacc cataggaaaa ggcgggcacg cttagtgagc ttcctgcggg     480

gagaggtttt tctgttagag ctggcanggt ctgctcatcg accatcttca ggcctcgtgc     540

c                                                                     541
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